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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David C. Schwartz, *et al.*

Date: March 2, 2010

Serial No.: 10/713,898

Art Unit: 1637

Filing Date: October 18, 2002

Examiner: Stephanie K. Mummert

Title: MICRO FLUIDIC SYSTEM FOR SINGLE MOLECULE IMAGING

Confirmation No.: 4216

File No.: 960296.99047

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**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

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**REQUEST FOR REVIEW**

In response to a final Office Action dated December 2, 2009, Applicants respectfully request consideration of the following remarks in connection with a Pre-Appeal Brief Request for Review. This paper accompanies a Notice of Appeal for the final Office Action and is being submitted before the filing of an appeal brief.

### **STANDING OF THE CLAIMS**

Claims 22 and 25 have been cancelled; Claims 1-20 and 28-33 have been withdrawn from consideration; Claims 21, 23, 24, 26 and 27 are pending and under consideration.

### **BRIEF SUMMARY OF THE INVENTION**

The claims under consideration are directed at methods of straightening and fixing polymeric molecules by (a) putting the polymeric molecules in a carrier liquid; (b) passing the polymeric molecules and carrier liquid through a micro-channel having a first wall electrostatically attractive to the polymeric molecule to promote a laminar flow of carrier liquid in the micro-channel that straightens the polymeric molecule over its length until at least the first and second ends of the molecule attach to the first wall; and (c) detaching the first wall from the micro-channel. In a final Office Action dated December 2, 2009, the Examiner in charge of the application committed clear errors of law and of fact in rejecting the claims, as discussed below.

### **ARGUMENTS**

**1. Because it was factual error to assert that a combination of the cited documents teaches or suggests the claimed invention, the Examiner's obviousness rejections are improper.**

The invention is nonobvious over Perkins and Bensimon because neither document, either alone or in combination, teaches or suggests using micro-channels or laminar flow. The Examiner rejected Claims 21, 23, 24 and 27 for alleged obviousness over Perkins *et al.*, in view of Bensimon *et al.* Claim 26 is rejected for alleged obviousness over Perkins, in view of Bensimon, and in further view of Kaiser. According to the Examiner, Perkins teaches elongating DNA molecules in laminar flow. In an attempt to align Perkins' teachings with the claimed method steps, the Examiner overstated what Perkins teaches. Perkins does not teach or suggest micro-channels (Office Action, page 6, line 11). Perkins teaches DNA tethered to latex microspheres, not to the wall of a micro-channel. Further, Perkins does not teach attachment of the length of the molecule to the micro-channel wall, as the Examiner alleged. Perkins' legend to Figure 1 and footnote 26 that the Examiner relied upon merely state that the molecule was tethered to a latex sphere at one end and deformed by constant fluid flow. In fact, Perkins

teaches attaching a DNA molecule to a microsphere at one end "while the other end remains free" (Perkins, page 83, right column, second paragraph). In contrast, Applicants' claims recite that at least the first and second ends of the molecule attach to the microchannel wall.

According to the Examiner, Bensimon teaches attaching the molecule to a first wall of the micro-channel (Office Action, page 6, fourth paragraph). However, Bensimon does not teach or suggest using micro-channels. Bensimon teaches using two cover slips to elongate polymeric molecules. Bensimon cannot teach or suggest attaching the molecule to a first wall of the micro-channel because Bensimon does not teach micro-channels in the first place.

Neither Perkins nor Bensimon teach using laminar flow. Applicants' invention employs laminar flow to straighten the polymeric molecule and to adhere it to the micro-channel wall. Perkins does not teach laminar flow. In fact, Perkins' microspheres create turbulence (Perkins, legend to FIG. 1B; page 84, right column) inconsistent with laminar flow. Bensimon teaches using capillary action/convection, principally caused by evaporation at a trailing edge of a liquid, to create a meniscus that aligns polymeric molecules attached to a surface (Bensimon, FIG. 6; Column 2, lines 59-68; Column 17, lines 41-45; Column 19, lines 30-32). Bensimon explicitly teaches away from using laminar flow, as explained below. Because neither Perkins nor Bensimon teach or suggest using laminar flow to elongate and fix polymeric molecules within micro-channels, and because Bensimon, in fact, teaches away from using laminar flow, a combination of these two documents cannot render obvious the claimed invention.

Kaiser does not compensate for the shortcomings of Perkins and Bensimon because Kaiser merely teaches treating polymeric molecules with a condensing agent. Kaiser contemplates neither laminar flow nor micro-channels.

For these reasons, Applicants' methods of straightening and fixing polymeric molecules using laminar flow of carrier liquid in a micro-channel that straightens the polymeric molecule until at least the first and second ends of the molecule attach to the micro-channel wall is nonobvious over Perkins, Bensimon, and Kaiser because none of these documents, either alone or in combination, teaches or suggests using micro-channels or laminar flow.

**2. Because it was legal error to disregard Perkins' and Bensimon's teaching away from the Examiner's proposed combination and modification of documents, the Examiner's obviousness rejections are improper.**

The documents cited by the Examiner explicitly teach away from the suggested combination and required modifications. Specifically, neither Perkins nor Bensimon teach or suggest using laminar flow, as explained above. Perkins teaches fluid flow that has turbulences caused by the microspheres. Bensimon teaches using capillary flow/convection. Paragraph [0050] of Applicants' specification explains the differences between capillary flow/convection and the laminar flow used in Applicants' invention. Bensimon goes further by expressly teaching away from using Applicants' laminar flow. Bensimon teaches that using the flow type used in Applicants' invention is not a good choice. Instead, Bensimon directs the reader to choose capillary flow/convection (Bensimon, Column 4, lines 7-20).

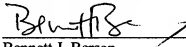
The Examiner admits that neither document teaches or suggests detaching the wall from the micro-channel to which the molecule is attached by at least two of its ends, but alleged that it was obvious to do so because Bensimon allegedly teaches analysis of a molecule stretched out on a surface. However, Perkins explicitly teaches away from adhering at least two of the molecule to a surface by stating that the molecule "was positioned away from any surface" (Perkins, page 83, second column, second paragraph, emphasis added). Also, Perkins expressly notes that the molecule is attached by only one end "while the other end remains free" (Perkins, page 83, right column, second paragraph).

Similarly, Bensimon merely teaches dipping two cover slips into a DNA-agarose solution and subsequently removing the cover slip from this solution. Bensimon does not teach micro-channels, much less removing a wall therefrom. Even if two cover slips were equivalent to a micro-channel, which they are not, Bensimon does not teach removing one from the other. Bensimon merely teaches removing both cover slips, unseparated, from a solution (Bensimon, Column 19, lines 21-26; passage relied upon by the Examiner, Office Action, page 8, second paragraph). The Examiner failed to explain how removing two cover slips from a solution makes obvious to one of skill in the art to remove the wall of a micro-channel.

**CONCLUSION**

Applicants submit that Claims 21, 23, 24, 26 and 27 recite patentable subject matter deserving of a timely notice of allowance. Applicants have introduced no new matter in making the above remarks. No fees beyond the fees authorized in the accompanying Notice of Appeal are believed due in connection with the submission of this Pre-Appeal Brief Request for review; however, if any fees are due, in this or any subsequent response, please charge Deposit Account 17-0055.

Respectfully submitted,



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